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Risk from Exposure to Polychlorinated Dibenzo-p-Dioxins and Dibenzofurans Emitted from Municipal Incinerators

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16. ABSTRACT

Incineration of wastes seems to be one of the major sources of PCDDs and PCDFs (dioxins). Their prevalence and extreme stability in the environment, bioavailability and bioaccumulation in the biota and human adipose tissues and breast milk are of much concern. 2,3,7,8-TCDD is one of the most toxic chemicals known and has been found to have teratogenic and carcinogenic activities in animals. Exposure to TCDD can result in chloracne, general weakness, drastic weight loss, hyperpigmentation of skin, hirsutism, porphyria cutanea tarda, liver damage, changes in activities of various liver enzymatic levels, abnormal lipid metabolism, abnormalities of the endocrine and immune systems, and possible teratogenic effects in humans. Moreover, chronic bioassay data indicate that TCDD is one of the most potent carcinogens known. It promotes liver and skin carcinogeneses, and is an initiator for various target organs in rodent test systems. According to the classification system of IARC, the qualitative evidence for carcinogenicity of TCDD is considered to be "sufficient" in animals and "inadequate " in humans. Consequently, TCDD has been placed in IARC's 2B category. In the absence of chronic bioassay data on other PCDDs and PCDFs, several TCDD equivalent approaches have been proposed for risk assessment on other congeners or mixtures. This paper compares the various approaches.

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RISK FROM EXPOSURE TO POLYCHLORINATED DIBENZO-*p*-DIOXINS AND DIBENZOFURANS EMITTED FROM MUNICIPAL INCINERATORS*

Debdas Mukerjee† and David H. Cleverly‡

(*Received December 1986, revised March 1986*)

Incineration of wastes seems to be one of the major sources of PCDDs and PCDFs (dioxins). Their prevalence and extreme stability in the environment, bioavailability and bioaccumulation in the biota and human adipose tissues and breast milk are of much concern. 2,3,7,8-TCDD is one of the most toxic chemicals known and has been found to have teratogenic and carcinogenic activities in animals. Exposure to TCDD can result in chloracne, general weakness, drastic weight loss, hyperpigmentation of skin, hirsutism, porphyria cutanea tarda, liver damage, changes in activities of various liver enzymatic levels, abnormal lipid metabolism, abnormalities of the endocrine and immune systems, and possible teratogenic effects in humans. Moreover, chronic bioassay data indicate that TCDD is one of the most potent carcinogens known. It promotes liver and skin carcinogeneses, and is an initiator for various target organs in rodent test systems. There is only a limited number of human epi-studies on carcinogenic outcome as a result of exposure to TCDD in isolated population.

According to the classification system of the International Agency for Research on Cancer (IARC), the qualitative evidence for carcinogenicity of TCDD is considered to be "sufficient" in animals and "inadequate" in humans. Consequently, this chemical has been placed in IARC's 2B category. A modification of the multistage model is utilized for extrapolating high-dose, two-year animal cancer bioassay data to estimate human cancer risk for long-term, low-dose human exposure. The upper limit of incremental cancer risk is 3.3×10^{-5} for a continuous lifetime exposure to 1 pg m^{-3} of TCDD in ambient air. With the exception of 2,3,7,8-TCDD and a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-HxCDDs, the chronic toxicity data on the rest of the 75 PCDD and 135 PCDF congeners are badly deficient. In the absence of chronic bioassay data on other PCDDs and PCDFs, several TCDD equivalent approaches have been proposed for risk assessment on other congeners or mixtures. This paper compares the various approaches.

Key Words—Dioxins, TCDD, TCDF, municipal incineration, health risk, isomer equivalents.

1. Introduction

Polychlorinated dibenzo-*p*-dioxins (PCDDs) and dibenzofurans (PCDFs) enter the environment as unwanted trace impurities in products derived from chlorinated phenols; 2,4,5-trichlorophenoxyacetic formulations, commercial mixtures of polychlorinated biphenyls, polychlorinated naphthalenes and through diverse combustion processes. PCDFs are also produced by overheated polychlorinated biphenyls in mal-

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† U.S. Environmental Protection Agency, Environmental Criteria and Assessment Office, Cincinnati, OH 45268, U.S.A.

‡ U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711, U.S.A.

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functioned transformers or capacitors. No known biogenic source, or any commercial use of PCDDs/PCDFs has yet been discovered. Municipal, industrial and other incinerators combusting organic materials and chlorinated compounds appear to be one of the major sources of PCDDs and PCDFs in the environment. The chlorinated-benzenes, -biphenyls and -phenols, which are present in high concentrations in emissions from waste incinerators, act either individually or in combination as precursors or intermediates of PCDDs and PCDFs. Tri- through octa-chlorinated homologous groups of PCDDs/PCDFs in stack emissions of municipal and industrial waste incinerators have been measured. A dilemma arises with respect to risk assessment as to how to evaluate the total PCDD and PCDF emissions in terms of toxicity when not every compound has yet been tested and is possibly not toxicologically equipotent.

PCDDs/PCDFs are highly lipophilic compounds and can easily bioaccumulate in fish, turtles, seals, terrestrial animals and even humans. Residues of these compounds have been detected in human adipose tissues and mothers' milk. Human exposure can occur via ingestion of fish from contaminated water bodies, contaminated meat or milk, or through inhalation or dermal contact. Human exposure has also occurred through occupational and accidental exposure to chemicals contaminated with PCDDs/PCDFs. 1,2,3,7,8-PeCDD has not been confirmed as a widespread contaminant in any commercial products but is always present in the emissions from waste incinerators. Detection of PCDD/PCDF residues, especially 1,2,3,7,8-PeCDD in mothers' milk indicate that the major source of exposure to these populations is occurring from municipal waste incinerator emissions (Rappe *et al.* 1984, Buser & Rappe 1984). Consequently, considerable concern has arisen over the public health impact of emissions of PCDDs/PCDFs from waste incinerators (see also Rappe *et al.* in this issue).

2. Toxicity of PCDDs and PCDFs

PCDDs/PCDFs (Dioxins) are members of a group of widely distributed and environmentally persistent compounds of which the 2,3,7,8-tetrachloro-dibenzo-*p*-dioxin (2,3,7,8-TCDD) isomer is one of the most toxic, teratogenic and carcinogenic chemicals known. The single oral dose, LD_{50}, of 2,3,7,8-TCDD in male guinea-pigs is 0.6 $\mu g\ kg^{-1}$ (Schewtz *et al.* 1973). There are only limited LD_{50} data on other PCDD/PCDF congeners. The LD_{50} values of seven PCDD congeners and three PCDF congeners in guinea-pigs are higher than 2,3,7,8-TCDD (Table 1). (Compare with Ahlborg & Victorin, Table 3, in this issue.)

TABLE 1
Estimated single oral LD_{50} for PCDDs and PCDFs in guinea-pigs

Congeners	LD_{50} ($\mu g\ kg^{-1}$)	Reference
2,3,7-TriCDD	29	McConnell *et al.* 1978
2,3,7,8-TCDD	0.6	Schwetz *et al.* 1973
1,2,3,7,8-PeCDD	3.1	McConnell *et al.* 1978
1,2,4,7,8-PeCDD	1125	McConnell *et al.* 1978
1,2,3,4,7,8-HxCDD	72.5	McConnell *et al.* 1978
1,2,3,6,7,8-HxCDD	70–100	McConnell *et al.* 1978
1,2,3,7,8,9-HxCDD	60–100	McConnell *et al.* 1978
1,2,3,4,6,7,8-HpCDD	>600	McConnell *et al.* 1978
2,3,7,8-TCDF	5–10	Moore *et al.* 1979
2,3,4,7,8-PeCDF	<10	McKinney & McConnell 1981
2,3,4,6,7,8-HxCDF	120	McKinney & McConnell 1981

2.1. *Mechanism of toxicity*

A number of reviews and comparative studies (Kimbrough 1974, Allen *et al.* 1979, McConnell & Moore 1979, Taylor 1979) clearly indicate that PCDDs and PCDFs elicit similar toxic and biological responses. They differ only in the degree of such responses. The exceptionally high and broad spectrum of 2,3,7,8-TCDD toxicity and other toxic congeners of PCDDs and PCDFs seem to be due to their distinctive mechanism of toxicity. Studies with genetically-inbred animals have demonstrated the role of aromatic hydrocarbon (Ah) regulatory gene (termed "Ah complex") and its gene product, the Ah cytosolic receptor protein (Nebert 1980, Nebert & Jansen 1979, Poland 1984), in their toxicity. Most of the toxic PCDDs and PCDFs elicit similar signs and symptoms of toxic effects in susceptible species that contain the Ah receptor protein (Carlstedt-Duke 1979, Carlstedt-Duke *et al.* 1979, 1981, Okey 1983, Mason & Okey 1982). The Ah-receptor protein interacts with TCDD and the resultant TCDD:Ah-receptor complex translocates into the nucleus, binds with DNA and activates specific mRNA (Carlstedt-Duke *et al.* 1981). Receptor binding is associated with the induction of aryl hydrocarbon hydroxylase (AHH) (Nebert 1980, Tukey *et al.* 1982).

2.2. *Structural activity relationship of PCDDs and PCDFs*

Recently, considerable interest has been generated on the effects of structure on the toxic and biological activity of PCDDs and PCDFs. Using the dextran charcoal receptor assay and ^{3}H-2,3,7,8-TCDD as the competing ligand, the relative binding affinities of 23 PCDD and PCDF congeners were first revealed by Poland *et al.* (1976). A correlation between the toxicity of PCDD congeners in guinea-pigs and mice (McConnell *et al.* 1978) and their AHH induction potencies in chick embryo and rat hepatoma H-4-II-E cells in culture and their binding affinities for mouse heptatic cytosolic receptor protein has been demonstrated (Poland *et al.* 1976, 1979, Bradlaw & Casterline 1979, Bradlaw *et al.* 1980). Structure–activity relationships have been reported for the PCDFs (Poland *et al.* 1979, Poland & Knutson 1982) and, like the PCDDs, there is some correlation among the toxicity of several individual PCDFs (Yoshihara *et al.* 1981), e.g. their binding affinities to male Wistar rat hepatic Ah-receptor site and AHH induction potencies in rat H-4-II-E hepatoma cells in culture (Bandiera *et al.* 1984*a*). The activity of the PCDD/PCDF ligand:Ah-receptor bond is a function of the geometric configuration of the compounds. Congeners with a chlorine substitution pattern at the four lateral positions (positions 2, 3, 7 and 8) and at least one vacant ring periposition (positions 1, 4, 6 and 9) of the molecule, have the greatest affinity for the Ah-receptor and the maximum inducibility of AHH activity. Additional chlorine substitution at positions 1, 4, 6 or 9 decreases AHH activity, and removal of one or more of the laterally attached chlorine atoms diminishes activity even further. One of the initial events of pathways in the mechanism of the biological activities of PCDDs/PCDFs seems to be stereospecific recognition and binding of these compounds by the Ah-receptor (Poland *et al.* 1979). Receptor binding assays and AHH induction assays have been established as useful indicators of the potency of individual PCDD/PCDF congeners relative to 2,3,7,8-TCDD (termed "TCDD equivalents"), as well as estimating the total potency of PCDD/PCDF as a complex mixture of the compounds. The utility of the TCDD equivalents approaches are supported by the apparent correlation of AHH induction and various *in vitro* biological activities with toxicity.

3. Health risk assessment of 2,3,7,8-TCDD

The rationale for assessment of public health risk from exposure to 2,3,7,8-TCDD has been discussed (Mukerjee *et al.* 1986, U.S. EPA 1985). Exposure to 2,3,7,8-TCDD can result in chloroacne and associated dermal abnormalities, thymic atrophy, severe body-weight loss, immunotoxicity, porphyria and other toxic effects.

From animal bioassay data (van Miller *et al.* 1977, Toth *et al.* 1979, Kociba *et al.* 1979, NTP 1980*a*) it can be concluded that 2,3,7,8-TCDD is an animal carcinogen. This bioassay data also indicate that 2,3,7,8-TCDD acts as an initiator for cancer of organs other than liver and skin. Observations by Pitot *et al.* (1980) and Poland *et al.* (1982) demonstrate its promotion action in liver and skin carcinogenesis in animals.

Epidemiologic observations by Hardell & Sandstrom (1979), Hardell & Ericksson (1981), Hardell *et al.* (1981), Eriksson *et al.* (1979, 1981), and Lynge (1985) supported by observations by Puntoni *et al.* (1986). Sarma & Jacobs (1981), Moses & Selikoff (1981), Bishop & Jones (1981) and Hoar *et al.* (1986) indicate that 2,3,7,8-TCDD is probably carcinogenic for humans and that exposure to it increases the incidence of soft tissue sarcoma and non-Hodgkin's lymphoma.

Using the available carcinogenic data on 2,3,7,8-TCDD from the study by Kociba *et al.* (1979), the cancer risk from exposure to 2,3,7,8-TCDD can be estimated by applying the modified multistage cancer model by Crump & Watson (1979). This model assumes that a cancer risk can be estimated for any dose of population exposure. Using this model, the slope of the dose–response relationship from the data of Kociba *et al.* (1979) was estimated and the 95% upper-limit carcinogenic potency for 2,3,7,8-TCDD was determined for humans to be 1.56×10^5 $(mg/kg/day)^{-1}$ (U.S. EPA 1985). The cancer risk for continuous lifetime 70-year exposure to an ambient air concentration of 1 pg m^{-3} of air of 2,3,7,8-TCDD has been estimated to be 3.3×10^{-5} (U.S. EPA 1985). In this estimation it was assumed that the breathing rate is 20 m^3 day^{-1} for an adult (70 kg man) and that 75% of the inhaled material will be absorbed. The linearized multistage model leads to a plausible upper-limit to the risk. This risk may not reflect the exact prediction of the risk. The range of risks is defined by the upper and lower limits and the lower limit may be as low as zero. The best or most probable estimates of risk can only be predicted when human data are utilized for assessing the risk and when exposures are in the dose range of the data. Consequently, U.S. EPA Cancer Risk Assessment Guidelines preclude the use of the statistical lower-bound estimate when extrapolating animal dose-response to a prediction of a likely response in human. The upperbound risk is used in order to err on the side of the protection of the public health.

Using the animal bioassay data on a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-HxCDD (NTP 1980*b*), the potency for HxCDD has been estimated as 6.2×10^3 $(mg/kg/day)^{-1}$ and lifetime cancer risk for an ambient concentration of 1 pg m^{-3} of a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-HxCDD to be 1.3×10^{-6} (U.S. EPA 1985).

4. TCDD equivalents approaches for risk assessment of total PCDDs and PCDFs

Except for 2,3,7,8-TCDD and a mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-HxCDD, there are no long-term chronic toxicity data for PCDD/PCDF congeners. Because of their prevalence in the environment, it is possible that other PCDD/PCDF congeners may add to the toxic burden caused by 2,3,7,8-TCDD. In the absence of any long-term chronic toxicity data, several schemes have been devised (in evaluating the exposure

from classes of PCDD and PCDF emissions from municipal waste incinerators) to derive the toxic equivalents (TCDD equivalents) based on AHH induction, Ah-receptor binding assays and other *in vitro* biological activities.

4.1. *Swiss approach*

The Swiss Federal Office for Environmental Protection (1982) devised a potency weighting system based on AHH induction to convert total tetrachlorinated through octachlorinated dioxins and furans into TCDD equivalents in the emissions of a municipal waste incinerator to facilitate risk assessment of exposure to all the reported chlorinated dioxin and furan homologues. When applied to emissions from a municipal waste combustor it seemed that the "2,3,7,8-TCDD equivalents" of the mixture of chlorinated dioxins and furans were approximately 60 times the actual amount of 2,3,7,8-TCDD measured in the emissions.

4.2. *Dutch approach*

Olie *et al.* (1983) devised a toxic equivalency method based on AHH induction to evaluate the magnitude of chlorinated dioxin and furan emissions from a municipal incinerator in The Netherlands. In this analysis, the TCDD equivalents were estimated to be 80 times the actual amount of 2,3,7,8-TCDD measured. Bioanalysis of fly ash collected from the electrostatic precipitor hopper to a municipal incinerator, as measured by the dose-dependent displacement of ^{3}H-2,3,7,8-TCDD bound to the Ah-receptor by the active congeners in the fly ash extract, showed the mixture of PCDDs and PCDFs to be at least 45 times more active than the concentration of 2,3,7,8-TCDD present by analysis.

4.3. *New York State approach, Eadon equivalents*

In an incident in which PCDD/PCDF contaminated soot emanating from a PCB-HCB transformer fire spread throughout the State office building in Binghamton, New York, the New York State Health Department applied an *in vitro* keratinization assay to soot extracts to evaluate dioxin-like biological activity. XB epithelial cells (derived from cloned mouse teratoma cells) exhibit a dose-dependent keratinization response to TCDD exposure when co-cultured with irradiated 3T3 cells (Eadon *et al.* 1983, Gierthy *et al.* 1984). Incubation of the soot extract with PCDD/PCDF congeners showed a correlation (0.89) between keratinization activity and the relative total dibenzofurans and dibenzodioxins present. The assay is apparently sensitive to only the most toxic compounds of the PCDDs and PCDFs and, therefore, provides a dose–response method of relating the potency of the extract to the inducible potency of 2,3,7,8-TCDD. By this method it was shown that 2,3,7,8-TCDF has about 1/20× the keratinization potential of 2,3,7,8-TCDD, and other PCDF isomers have even lower activity. The dibenzofurans and PCDDs without substitution at any of the four lateral positions were sufficiently inactive to warrant little concern based upon comparison of the keratinization ability of 2,3-, 2,7-, 1,6-, 1,3,6,8-, 1,3,7,8- and 2,3,7-chlorodibenzodioxins to 2,3,7,8-TCDD. It was observed in the assay that the majority of biologically active isomers were members of the tetra- and penta-chlorinated homologues. The assay permitted the researchers to develop a scale of biological activity of various congeners relative to the keratinization potential of 2,3,7,8-TCDD (Eadon equivalents).

4.4. *U.S. EPAs interim approach*

Many compounds of PCDD and PCDF have been compared to the potency of 2,3,7,8-TCDD utilizing *in vitro* biological activity assays, e.g. AHH enzyme activity in rat hepatoma cells and chick embryo liver, ALA synthetase in chick embryo liver, and keratinization of XB/3T3 mouse teratoma cells. These have been reviewed by Kociba & Cabey (1985). From these enzyme-induction and cell-transformation assays it is possible to predict the toxic potency of 2,3,7,8-substituted congeners of these compounds, relative to the known potency of 2,3,7,8-TCDD. Bellin & Barnes (1987) and Barnes *et al.* (1986) incorporated this information into a calculation of TCDD equivalents, for using the scheme in hazard assessment of dioxin-contaminated waste and/or commercial products contaminated with a complex mixture of dioxin and furan compounds. Basically, TCDD equivalents are calculated using a Relative Potency Factor (RPF) or Toxic Equivalence Factor (TEF) derived from the various assays. When the isomer-specific concentration or homologue concentration of PCDD/PCDF are multiplied by the TEF the product is a concentration of TCDD equivalents that may be regarded as equipotent to 2,3,7,8-TCDD. Table 2 shows the RPF to be used when specific analyses of isomers are quantified.

TABLE 2

Comparison of the U.S. EPA (Bellin & Barnes 1987) and the method proposed by Safe (1986) to estimating relative toxicity of PCDDs and PCDFs

Congeners	U.S. EPA (Barnes & Barnes 1987)	Safe (1986)
Mono- to tri-	0	0
	0	0
2,3,7,8-TCDD	1	1
Other TCDDs	0.01	0.001
2,3,7,8-PeCDDs	0.5	0.01
Other PeCDDs	0.005	0.006
2,3,7,8-HxCDDs	0.04	0.03
Other HxCDDs	0.0004	—
2,3,7,8-HpCDDs	0.001	—
Other HpCDDs	0.0001	—
OCDD	0	0.0002
2,3,7,8-TCDFs	0.1	0.2
Other TCDFs	0.001	0.004
2,3,7,8-PeCDFs	0.1	0.3
Other PeCDFs	0.001	0.01
2,3,7,8-HxCDFs	0.01	0.2
Other HxCDFs	0.0001	—
2,3,7,8-HpCDFs	0.001	—
Other HpCDFs	0.00001	—
OCDF	0	—

4.5. *Ontario province, Canada approach*

The Ministry of Labor of the Ontario Government, Canada (1982) has developed a risk assessment guideline for complex mixtures of compounds of dioxins and furans in water, air and soil samples. The guidelines involve the utilization of Toxic Equivalent Factors (TEFs) based on AHH induction in rat hepatoma cells, *in vitro*. In their evaluation of airborne emissions of PCDDs/PCDFs they assume (based on experience in source testing) that 2,3,7,8-TCDD is 5–6% of total tetra-CDD emissions. Thus, when using the TEFs they first subtract the estimated 2,3,7,8-TCDD from the tetra-CDD homologue.

4.6. *Approach proposed by Safe (1986)*

Mason *et al.* (1985) correlated the *in vitro* AHH-inducing potency of PCDFs with the thymic atrophy or body-weight loss caused by each congener in rodents. Although this is an obvious oversimplification of the problem, it may be accepted as a good model when a rapid indication of the potential toxicity of new congeners is needed.

Bradlaw and Casterline (1979), working with rat hepatoma cell culture (as a rapid screen test for detecting minute (pg) amounts of certain classes of compounds, e.g. PCDFs, PCDDs and PCBs), found that AHH activity was induced by PCDF containing at least three or four lateral ring positions substituted by chlorine atoms in the ring positions 2, 3, 7 and 8; congeners with two or less chlorine atoms in the lateral positions showed no inductive effect up to a dose of 5 or 10 mg kg^{-1} body weight.

The quantitative *in vitro* data reported by Bandiera *et al.* (1984*b*) and Mason *et al.* (1985) demonstrate the relationship between the different PCDDs and PCDFs in their AHH and EROD-inducing potency. Bandiera *et al.* (1984*b*) showed that the AHH inductive ratios of the 2,3,4/1,3,8, 2,6,7/1,3,8, and 2,3,4,6/1,2,4,8 pairs of PCDF isomers were 1, 2, 8, 7 and 9, respectively.

The $-\log EC_{50}$ values for *in vitro* AHH inducing potencies versus the $-\log ED_{50}$ values for body-weight loss and thymic atrophy for a series of PCDF congeners have been plotted (Safe 1986). Statistical analysis of the plots showed an excellent correlation, corroborated by the fact that the compounds tested differed widely in both *in vivo* and *in vitro* biological activities and toxic potencies. 2,3,7,8-TCDC was the most active AHH inducer *in vitro* and the most powerful and toxic congener *in vivo*. Comparison of this approach with that of the U.S. EPA (Table 2) indicate that these two approaches give more or less similar values.

4.7. *Swedish approach*

The current Swedish approach, using Eadon equivalents, to estimate the toxicity and health risk of dioxins is summarized by Ahlborg (in this issue) including a comparison of some of the existing equivalents.

5. Evaluation of TCDD equivalents approach for risk assessment

The aforementioned rank ordering of the potency of various PCDD/PCDF congeners based mostly on induction of enzyme activity or keratinization assays provides a means of estimating, albeit crudely, the toxicological significance of exposure to a complex array of these compounds. This is especially important in view of the fact that most of

these compounds have not been asssayed for teratogenic, carcinogenic, or other chronic effects. Thus, these various methods of rank ordering potency in relation to 2,3,7,8-TCDD may provide a reasonable means even though not fully supported by scientific data to assess the risk of cancer to populations exposed to chronic and dispersive emissions of PCDDs/PCDFs from stationary combustion sources. This is important to regulators who need to estimate a hazard now, without having to wait perhaps several years for the results of animal bioassays. Various schemes utilizing the notion of toxic equivalency to 2,3,7,8-TCDD are based primarily on microsomal mono-oxygenase activity.

Co-administration of a non-toxic or non-inducing dose of 2,3,7,8-TCDF can decrease the AHH induction and immunotoxicity of 2,3,7,8-TCDD (Rizzardini *et al.* 1983). A molecule with low toxicity but high affinity for the Ah-receptor may possibly offer protection against the toxicity of 2,3,7,8-TCDD. Furthermore, age and sex-related decreases in the mixed function oxidase (MFO) activity is associated with increased 2,3,7,8-TCDD lethality (Beatty *et al.* 1978). This suggests that reduced MFO activites may enhance 2,3,7,8-TCDD toxicity.

The major shortcomings of utilizing the microsomal mono-oxygenase activity assays in risk assessment to airborne emissions of chlorinated dioxins and dibenzofurans are:

(1) enzyme induction has not been directly linked with carcinogenicity, or any other chronic toxicologic endpoint;
(2) elucidation of specific intranuclear events leading to transcription of specific mRNAs, and translation of mRNAs into enzyme induction remains unknown;
(3) the ultimate biochemical lesion of the proposed mechanism of toxicity is unknown;
(4) the concentration of the Ah-receptor in various human tissues has not been fully investigated, nor has a toxic response in humans been correlated with enzyme induction. Hypothyroidism, observed in animals exposed to 2,3,7,8-TCDD is possibly involved in the manifestations of a spectrum of pathological conditions (Bastomsky 1977). The partial protection from 2,3,7,8-TCDD induced wasting syndrome and immunotoxicity as a result of thyroidectomy (Rozman *et al.* 1984, Pazdernik & Rozman 1985) seems not to be mediated through any change in the liver Ah-receptor regulated processes (Henry & Gasiewicz 1986);
(5) photolysis of higher chlorinated PCDDs/PCDFs can result in ultimate dechlorination of the molecule (Choudhury & Hutzinger 1982). However, there is some possibility of highly toxic 2,3,7,8-TCDD formation due to photolysis of 2,3,4,7,8,9- and 1,2,3,7,8,9-HxCDDs (Buser 1979) if these compounds are emitted from the incinerators.

These shortcomings suggest that using TCDD equivalent approaches for risk assessments may result in underestimation of risk.

Lack of complete elucidation should not, however, preclude the regulator from developing risk assessment methodologies based on AHH induction or receptor-binding assays as a reasonable means of estimating the hazard of exposure to a complex mixture of PCDDs/PCDFs from emissions of stationary combustion sources. The responsibility of the regulator is to manage risk to the exposed population even before all the scientific information is available. Thus toxic equivalency schemes can be used as an interim basis of assessing risk to the exposed population residing near emitters of PCDDs and PCDFs.

6. Risk assessment of PCDD/PCDF emissions from selected U.S. incinerators

6.1. *Earlier approach*

In 1981 the U.S. Environmental Protection Agency issued a report evaluating the health risks associated with exposure to emissions of a homologous mixture of tetrachlorinated dibenzo-*p*-dioxins (TCDD) from five municipal solid waste heat recovery incinerators of various size and design (U.S. EPA 1981). Specific speciation of only one congener, 2,3,7,8-TCDD, was accomplished leaving risk assessors with the dilemma of how to evaluate risk of perhaps 21 other toxic dioxin compounds comprising the class of TCDD. Of the five facilities sampled, only one (Chicago, NW) provided speciation data of 2,3,7,8-TCDD with sufficient analytical confidence to compare with

TABLE 3

Comparison of 2,3,7,8-TCDD toxic equivalency methods in determining risk from population exposure to CDD/CDF emissions from a heat recovery massburn MWC operating in Westchester, New York *

Compound	Conc.†	EPA TEFs	NY TEFs	Ontario Canada	Swiss TEFs	EPA TE	NY TE	Can. TE	Swiss TE
2,3,7,8-TCDD	3.65	1	1	1	1	3.65	3.65	3.65	3.65
Other TCDD	33.00	0.01	0	0.01	0.01	0.33	0	0.33	0.33
1,2,3,7,8-PeCDD	9.38	0.5	1	0.1	0.1	4.69	9.38	0.94	0.94
Other PeCDD	27.17	0.005	0	0.001	0.1	0.14	0	0.03	2.72
1,2,3,4,7,8-HxCDD	4.47	0.04	0.03	0.1	0.1	0.18	0.13	0.45	0.45
1,2,3,6,7,8-HxCDD	0.14	0.04	0.03	0.1	0.1	0.01	0.00	0.01	0.01
1,2,3,7,8,9-HxCDD	1.55	0.04	0.03	0.1	0.1	0.06	0.05	0.02	0.16
Other HxCDD	43.91	0.0004	0	0.001	0.01	0.02	0	0.04	0.44
Total HpCDD	71.77	0.001	0	0.01	0.01	0.07	0	0.72	0.72
Total OCDD	115.4	0	0	0.0001	0	0	0	0.01	0
2,3,7,8-TCDF	27.89	0.1	0.33	0.5	0.1	2.8	9.2	14.0	2.79
Other TCDF	358.7	0.001	0	0.005	0.1	0.36	0	1.8	35.9
1,2,3,7,8-PcDCF	51.2	0.1	0.33	0.5	0.1	5.12	16.9	25.6	5.12
2,3,4,7,8-PcCDF	30.2	0.1	0.33	0.5	0.1	3.02	10.0	15	3.02
Other PcCDF	145.2	0.001	0	0.005	0.1	0.15	0	0.73	14.5
1,2,3,4,7,8-HxCDF	19.0	0.01	0.01	0.1	0.1	0.19	0.19	1.9	1.9
1,2,3,7,8,9-HxCDF	1.01	0.01	0.01	0.1	0.1	0.01	0.01	0.1	0.1
2,3,4,6,7,8-HxCDF	5.29	0.01	0.01	0.1	0.1	0.05	0.05	0.53	0.53
Other HxCDF	248.5	0.001	0	0.001	0.1	0.25	0	0.25	24.9
Total HpCDF	135.9	0.001	0	0.01	0	0.14	0	1.36	0
Total OCDF	4.98	0	0	0.0001	0	0	0	0	0
Total ground-level concentration of 2,3,7,8-TCDD Equivalents (10^{-15} gm m^{-3})						21.24	49.6	67.5	98.2

	EPA	NY	Can.	Swiss
Maximum individual lifetime cancer risk (10^{-6})	1	2	2	3

* *Description of the incinerator:* Heat Recovery Massburn waterwall MWC: capacity, 2000 tonne day^{-1}; operating temperature, 900°C; steam generated, 228,202 kg h^{-1}.

† Maximum ground-level concentration of specific CDDs/CDFs in femtograms m^{-3} of air.

TABLE 4

Comparison of 2,3,7,8-TCDD toxic equivalency methodologies in determining maximum individual lifetime risk from exposure to CDDs/CDFs in the emissions of a non-heat recovery massburn municipal waste combustor operating in Philadelphia, Pennsylvania *

Compound	Emissions ($\mu g\ s^{-1}$)	EPQ TEFs	NY TEFs	Can. TEFs	Swiss TEFs	EPA TE	NY TE	Can. TE	Swiss TE
2,3,7,8-TCDD	0.14	1	1	1	1	0.14	0.14	0.14	0.14
Other TCDD	4.26	0.01	0	0.01	0.01	0.043	0	0.04	0.04
1,2,3,7,8-PeCDD	1.10	0.5	1	0.1	0.1	0.55	1.1	0.11	0.11
Other PeCDD	8.90	0.005	0	0.001	0.1	0.045	0	0.01	0.89
1,2,3,4,7,8-HxCDD	2.50	0.04	0.03	0.1	0.1	0.1	0.08	0.25	0.25
1,2,3,7,8,9-HxCDD	2.50	0.04	0.03	0.1	0.1	0.1	0.08	0.25	0.25
1,2,3,6,7,8-HxCDD	2.50	0.04	0.03	0.1	0.1	0.1	0.08	0.25	0.25
Other HxCDD	10.50	0.0004	0	0.001	0.01	0.004	0	0.01	0.11
1,2,3,4,6,7,8-HpCDD	3.30	0.001	0	0.01	0.01	0.003	0	0.03	0.03
Other HpCDD	3.00	0.00001	0	0.0001	0.01	†	0	0	0.03
2,3,7,8-TCDF	0.35	0.1	0.33	0.5	0.1	0.035	0.12	0.18	0.04
Other TCDF	6.55	0.001	0	0.005	0.1	0.007	0	0.03	0.66
1,2,3,7,8-PeCDF	0.39	0.1	0.33	0.5	0.1	0.039	0.13	0.20	0.04
2,3,4,7,8-PeCDF	0.52	0.1	0.33	0.5	0.1	0.052	0.17	0.26	0.05
Other PcCDF	9.09	0.001	0	0.005	0.1	0.009	0	0.05	0.91
1,2,3,4,7,8-HxCDF	2.50	0.01	0.01	0.1	0.1	0.025	0.03	0.25	0.25
1,2,3,7,8,9-HxCDF	1.38	0.01	0.01	0.1	0.1	0.013	0.01	0.14	0.14
1,2,3,6,7,8-HxCDF	0.25	0.01	0.01	0.1	0.1	0.003	0.003	0.03	0.03
2,3,4,6,7,8-HxCDF	1.38	0.01	0.01	0.1	0.1	0.013	0.01	0.14	0.14
Other HxCDF	12.49	0.0001	0	0.001	0.1	0.001	0	0.01	2.35
1,2,3,4,6,7,8-HpCDF	4.40	0.001	0	0.01	0.1	0.004	0	0.04	0.44
1,2,3,4,7,8,9-HpCDF	0.35	0.001	0	0.01	0.1	†	0	0.004	0.04
Other HpCDF	1.50	0.00001	0	0.0001	0.1	†	0	†	0.15
OCDD	2.5	0	0	0.0001	0	0	0	†	0
OCDF	0.50	0	0	0.0001	0	0	0	†	0
2,3,7,8-TCDD equivalent emissions ($\mu g\ g^{-1}$)						1.29	2	2.4	6.2
2,3,7,8-TCDD equivalent ground-level concentration pg m^{-3}						1.2	1.6	2.0	5.1
Maximum individual lifetime cancer risk (10^{-6})						40	50	70	170

* Description of the incinerator: refractory lined massburner municipal incinerator; no heat recovery; capacity, 682.5 tonne day^{-1}; maximum operating temperature, 1100°C.
† Measurements of emissions were too low to result in toxic equivalent emissions.

the abundance of TCDD. At the Chicago plant, 2,3,7,8-TCDD constituted about 7% of the total tetrachlorinated dioxin emissions (Haile & Stanley 1983). The agency, in undertaking a risk assessment, assumed that all the TCDDs were as carcinogenic as the 2,3,7,8-TCDD congener and, therefore, the emission of a mixture of TCDD compounds was 14 times more potent than the actual concentration of 2,3,7,8-TCDD present in stack emissions (Barnes 1983). Thus, the agency reduced the analysis of perhaps as many as 22 separate compounds of tetrachlorine-substituted dioxin to an equivalent toxicity of 2,3,7,8-TCDD. The maximum annual average ground-level concentration of total TCDD was 0.092 pg m^{-3} and this was treated as total 2,3,7,8-

TCDD. Applying the unit risk factor for 2,3,7,8-TCDD to the linearized multi-stage model of the toxic equivalents concentration indicated an upper bound individual risk of cancer to be 8×10^{-6}.

The agency used an identical procedure in evaluating the risks from TCDD exposure in emissions in the Hampton, Virginia incinerator (Cook 1983). The maximum annual ground-level concentration of total TCDD was found to be 0.51 pg m^{-3}. Using the same risk model, the upper limit individual risk of cancer of exposure to the 2,3,7,8-TCDD toxic equivalents was determined to be 4.6×10^{-5}. Thus, the emission of 2,3,7,8-TCDD toxic equivalents from the Hampton, Virginia incinerator produced an individual lifetime risk of cancer approximately six times greater than emissions from the Chicago, NW incinerator.

6.2. *Current approach*

Regulatory authorities in Sweden, Denmark, Norway, The Netherlands, Switzerland, West Germany, Canada and the U.S.A. have recognized the utility of "TCDD equivalents" risk-assessment procedures in generating probabilistic estimates of public health risk posed by the mixtures of PCDD/PCDF compounds characteristic of incinerator emissions. Of particular interest to the community of environmental managers is whether agreement exists among the wide variety of toxic equivalency procedures in terms of predicting carcinogenic risk to the population exposed to incinerator emissions. To investigate this question we have selected the PCDD/PCDF emissions measured at a modern energy recovery municipal waste combustor to serve as an example of the risk prediction resulting from application of the various toxic equivalency procedures. Tables 3 and 4 show the comparative results of various procedures when specific isomers of PCDD/PCDF have been quantified in the emission. Table 5 makes the comparison when only homologue data are available. As can be seen in Table 3 all the various procedures predict a 10^{-6} maximum lifetime risk to individuals exposed continuously for 70 years to the predicted maximum ground-level concentra-

TABLE 5

Comparison of toxic equivalency methodologies where only homologue data are available: CDD/CDF emissions from a heat-recovery massburn MWC in Westchester, New York

Compound	Conc. ($fg\,m^{-3}$)	EPA TEFs	NY TEFs	Ontario Canada	Swiss TEFs	EPA TE	NY TE	Can. TE	Swiss TE
2,3,7,8-TCDD	3.65	1	1	1	1	3.65	3.65	3.65	3.65
Other TCDD	33.00	0.01	0	0.01	0.01	0.33	0	0.33	0.33
Total PeCDD	36.55	0.5	1	0.1	0.1	18.3	36.55	3.66	3.66
Total HxCDD	50.07	0.04	0.03	0.1	0.1	2.0	1.5	5.00	5.00
Total HpCDD	71.77	0.001	0	0.01	0.01	0.7	0	0.72	0.72
OCDD	115.4	0	0	0.0001	0	0	0	0.01	0
Total TCDF	386.6	0.1	0.33	0.5	0.1	38.7	127.58	193.3	38.66
Total PeCDF	226.6	0.1	0.33	0.5	0.1	22.7	74.78	113.3	22.66
Total HxCDF	233.8	0.01	0.01	0.1	0.1	2.34	2.34	23.38	23.38
Total HpCDF	135.9	0.001	0	0.01	0.1	0.14	0	1.36	13.59
OCDF	4.98	0	0	0.0001	0	0	0	0.00	0
Total 2,3,7,8-TCDD equivalents						88.23	246.4	344.7	111.65
Maximum individual lifetime risk (10^{-6})						3	8	11	4

tion of 2,3,7,8-TCDD equivalents. The procedures differ from the prediction of the U.S. EPA by a factor of 2–3. However, given the uncertainties inherent in predicting the public health risk, there is generally good agreement in estimating risk. As can be seen in Table 5, the toxic equivalency procedures do predict high risk associated with the same incinerator emissions when only homologue data are used. This increase in risk is on a range of three-fold for the EPA procedure and up to five-fold for the Canadian procedure. However, one should not conclude that isomer-specific data gives more precise measure of health risk than homologue data, because there may be additional halogenated isomers manifesting similar toxicity that are not considered in the risk-assessment procedures. For example, tri- or di-chlorinated PCDDs/PCDFs may be tested in whole animals and be shown to elicit a similar toxic response as 2,3,7,8-TCDD. Likewise, the mechanism of toxicity for this family of compounds has yet to be elucidated fully.

7. Conclusions

Various estimates of health risks from emissions from municipal incinerators are compared and the reasoning behind the current U.S. EPA methods for evaluating such risks are described. One should not be intellectually seduced into believing that these methodologies are truly accurate in their prediction of risk. Much more needs to be discovered concerning the macromolecular pathways of carcinogenesis, teratogenesis and other chronic diseases associated with these compounds before more scientifically reliable statements of risk can be made. Until we are more knowledgeable in this matter, a concept of TCDD equivalency is at best considered as a predictive tool for risk managers to evaluate the atmospheric emissions of PCDD/PCDF mixtures for combustion sources.

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